## REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 180-189 will be active in the application subsequent to entry of this Amendment.

The Official Action raises issues with respect to claim clarity and enablement of disclosure as well as rejections directed to a limited number of claims on the basis of prior art. Applicants address these objections and rejections noting that claims 185-189 are free of the prior art and that claim 187 is rejected only as being dependent from a rejected claim.

Discussion of Claim Amendments

The claims have been amended as set out in the accompanying set of claims.

Claim 180 has been amended by referring to "resorbable or bio-erodible" rather than "corrodible".

Claim 184 has been amended to reflect the language used on page 7, lines 20-22, as suggested by the Examiner.

Claim 185 has been amended as suggested by the Examiner with reference to page 5, line 18.

Claim 187 has been made dependent on claim 186.

Claim 189 has been amended as suggested by the Examiner by referring to a platinum anti-cancer substance.

Response to Claim Rejections - Section 112

Claim 180

Claim 180 has been amended as suggested by the Examiner.

Claims 181-183

The Examiner considers that there is no basis for the claimed porosity ranges and values in claims 181-183. This is not the case. Lines 18 and 19 on page 3 state that "The porous silicon may have a porosity that is in a range between any two of the figures mentioned above."

The values 2%, 4%, 30%, 50% and 80% set out in these claims are specifically disclosed and fall within the "any two of the figures set out above" criteria established in the description. The rejection of these claims is erroneous as they are fairly based on the description of the invention.

Claim 184

As requested by the Examiner, the language used on page 7, lines 20-23 has been included in claim 184.

Claim 185

Claim 185 has been amended by adopting the language used on page 5, line 18 of the description.

Claim 186

With regard to claim 186, the atomic percentage is a clear term. For example, suppose that the element (e.g. phosphorus) is present at a concentration of 1 atomic % in mesoporous silicon at a particular depth, this would mean on average there would be 1 phosphorus atom for every 100 silicon atoms present per unit volume at that depth. Attention is directed to page 31, line 25 of the description which states that the atomic percent is a concentration. Concentrations are always quantities per unit volume (claim 186 already includes the word "concentration").

Claim 187

Claim 187 has been made dependent on claim 186.

Claim 188

The Official Action suggests "phosphorus is not disclosed" in the description. This is not so. Page 13 of the description at lines 19 and 20 refers to Figure 5 which shows a table of elements which may be administered using the present invention - phosphorus is included. Also, reference may be made to parts (b) and (c) on pages 15/16 and the subsequent trials.

Claim 189

Claim 189 has been amended by referring to a platinum anti-cancer substance as suggested by the Examiner.

Response to Lack of Novelty Rejection

Claims 180-184 only have attracted rejections based upon prior art. The remaining claims, that is claims 185-189 are therefore free of the prior art. Applicants have addressed the examiner's issues with regard to claim clarity and antecedent basis and submit that claims 185-189 are in condition for allowance. The remaining comments are directed to claims 180-184 and the examiner's continued refusal to acknowledge patentability of these claims.

The Examiner has rejected claims 180-184 in light of WO 97/06101 (WO '101). The Examiner considers that WO '101 does not explicitly disclose resorbable silicon but because of the inherent characteristics of the materials described in WO '101, then they must be resorbable.

However, the Examiner's arguments fail to recognize that applicants are not claiming a resorbable porous silicon sample, applicants are claiming a method of administering a beneficial substance comprising the use of a resorbable mesoporous silicon sample and the method comprises subcutaneous implantation. Again, applicants' claims are directed to methods of treatment not articles. The examiner has failed to acknowledge that the claims require subcutaneous implantation.

Clearly, WO '101 does not disclose a method of delivering a beneficial substance to a human or animal subject subcutaneously. Also, WO '101 does not disclose a method of delivering a beneficial substance to a human or animal subject subcutaneously using resorbable mesoporous silicon. This rejection is deficient on its face and should be withdrawn.

Response to "Obviousness" Rejection

The Examiner has rejected claims 180-184 for being "obvious" over WO '101.

WO 97/06101 (Canham) does not disclose a method of delivering a beneficial substance to a human or animal subject subcutaneously. By way of background, the subcutaneous layer (sometimes referred to as the subcutis) is the layer of tissue directly underlying the cutis (the two outer layers of skin) and is mainly composed of adipose tissue. Its physiological function includes insulation and storage of nutrients. It is known to administer injections subcutaneously.

In addition, Canham does not disclose a method of delivering a beneficial substance to a human or animal subject subcutaneously using resorbable mesoporous silicon.

Canham centers around the ability of silicon to form bonds with bone. The ability of silicon to form bonds with bone means the silicon is bioactive.

The precise nature of the silicon is important in determining whether or not a bond will form between the silicon and bone. It is likely that the silicon has to be in a form which gives it the ability to form nucleation sites for the formation of calcium phosphate which in turn forms hydroxyapatite (the inorganic phase of bone).

Put another way, Canham illustrates a form of bioactivity wherein calcification results. For example, Figure 3 illustrates the formation of apatite (region C) indicating the ability of the

silicon to bond to bone. Hence Canham clearly illustrates that certain silicon samples are useful at skeletal sites. The subcutaneous layer is not a skeletal site.

The present invention is concerned with the delivery of beneficial substances, such as drugs, following implantation in the subcutaneous layer, in other words at soft tissue sites. If these subcutaneously implanted samples were to calcify in the proximity of soft tissue, then this would give rise to significant problems. Firstly, calcification in a soft tissue environment is undesirable from a toxicology standpoint. Further, in-vivo deposition of calcium phosphate coatings will impede silicon resorption and will inhibit drug delivery.

The present invention centers around the finding that mesoporous silicon can resorb following implantation in the subcutaneous layer. This would not have been obvious from the teaching of Canham

The (apparent) most relevant sections of Canham, at least so far as the Examiner is concerned, are possibly the final paragraph on page 12 and lines 20-24 of page 17. Applicants address these passages as follows:

Canham, page 12, final paragraph

A mesoporous porous silicon sample was immersed in Simulated Body Fluid (SBF). After one day the sample had been dissolved by the SBF. Such a result does not provide an indication of how such a sample would behave when implanted in the subcutaneous layer. In addition, the teaching of Canham in its entirety would suggest that, in all likelihood, calcification would also occur.

Canham, page 17, lines 20-24

This section in Canham presents the case that the experiments which have been carried out in Simulated Body Fluid do not necessarily provide a clear indication of the suitability of a particular form of porous silicon for resorbable material applications and that it may be necessary to carry out in-vivo experiments to determine whether a particular desired physiological response is achieved.

In other words, this section acknowledges that the results in SBF are interesting, they do not necessarily provide a reliable model for particular sites in the body. In other words, a reasonable expectation is not provided by the Canham reference. There is no suggestion in Canham to use mesoporous silicon in the subcutaneous layer.

There are a broad range of physiological environments in the body which provide very different environments and therefore different challenges in developing a sample of silicon which will be suitable for use in a particular environment.

As will be apparent to any researcher working in the drug delivery field, huge resources in the pharmaceutical industry are needed in developing different forms of a drug for different administration routes. Simulated Body Fluid (SBF) is significantly different from the fluid found in the subcutaneous layer. The main fluid found in the subcutaneous layer is human plasma. Human plasma is a complex mixture of constituents which, unlike SBF, comprises hugely complex materials such as cells and proteins. It is difficult to predict how a material such as porous silicon will interact with these complex biological molecules. The skilled person on reading Canham might expect that that some calcification would occur and a bond would start to form between the cells and proteins in the human plasma and the porous silicon. This would seriously inhibit the efficacy of the implant.

On the basis of this argument alone, it is considered that the claims of the present invention are inventive over Canham. However, it is also worth considering a comparison of some of the experimental results in the present application over Canham.

Comparison of experimental results

Figures 2A-2D of the present application show scanning electron micrographs of a 30% mesoporous silicon subcutaneous implant explanted from a guinea pig at 0,1, 4 and 12 weeks after implant (see page 13, lines 5-7 and page 14, lines 17-22).

As set out in the present application on page 14, lines 17-22, Figures 2A-2D clearly show that there was considerable corrosion of the subcutaneous porous silicon.

Page 17 (first paragraph) of the present application goes on to describe how the 12 week tests were followed by a 26 week study which showed entirely consistent results. There was a steady corrosion of porous silicon and the corrosion of the implants did not cause any significant harmful effects on the test subjects. There was no gross inflammatory response, no significant fibrotic scarring, and excreting the corroded silicon was not a problem.

These results illustrate how steady and continuous the rate of corrosion can be when porous silicon is implanted subcutaneously. In other words, it is suitable for the delivery of drugs over a significant period of time which is crucially important for subcutaneous delivery of drugs.

This could not have been predicted from the teaching of Canham. The teaching in Canham at page 12 is that in SBF the porous silicon sample is dissolved in a single day.

In summary, there are a number of persuasive components of applicants' position: First of all, the teaching of Canham would mean the skilled person would have no insight into the suitability of using porous silicon for subcutaneous implantations. There is no suggestion by Canham to use porous silicon in such a mode of delivery. From a fair reading of Canham, the skilled person could also have reasonably expected that calcification of the porous silicon would have occurred in-situ which would have meant subcutaneous delivery was not realistically possible. Finally, the immersion of porous silicon in SBF in Canham resulted in a rate of corrosion which would not motivate the skilled person to consider that mesoporous silicon would be suitable for subcutaneous implantation.

For the various reasons set out in the response of July 10, 2007 (and previous submissions), the amended claims are also inventive over WO '101.

Essentially, the present invention as currently claimed centers around the finding that mesoporous silicon can resorb following implantation in the subcutaneous layer. This would not have been obvious from the teaching of WO '101. There are a broad range of physiological environments in the body which provide very different environments and therefore different challenges in developing a sample of silicon which will be suitable for use in a particular environment.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

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